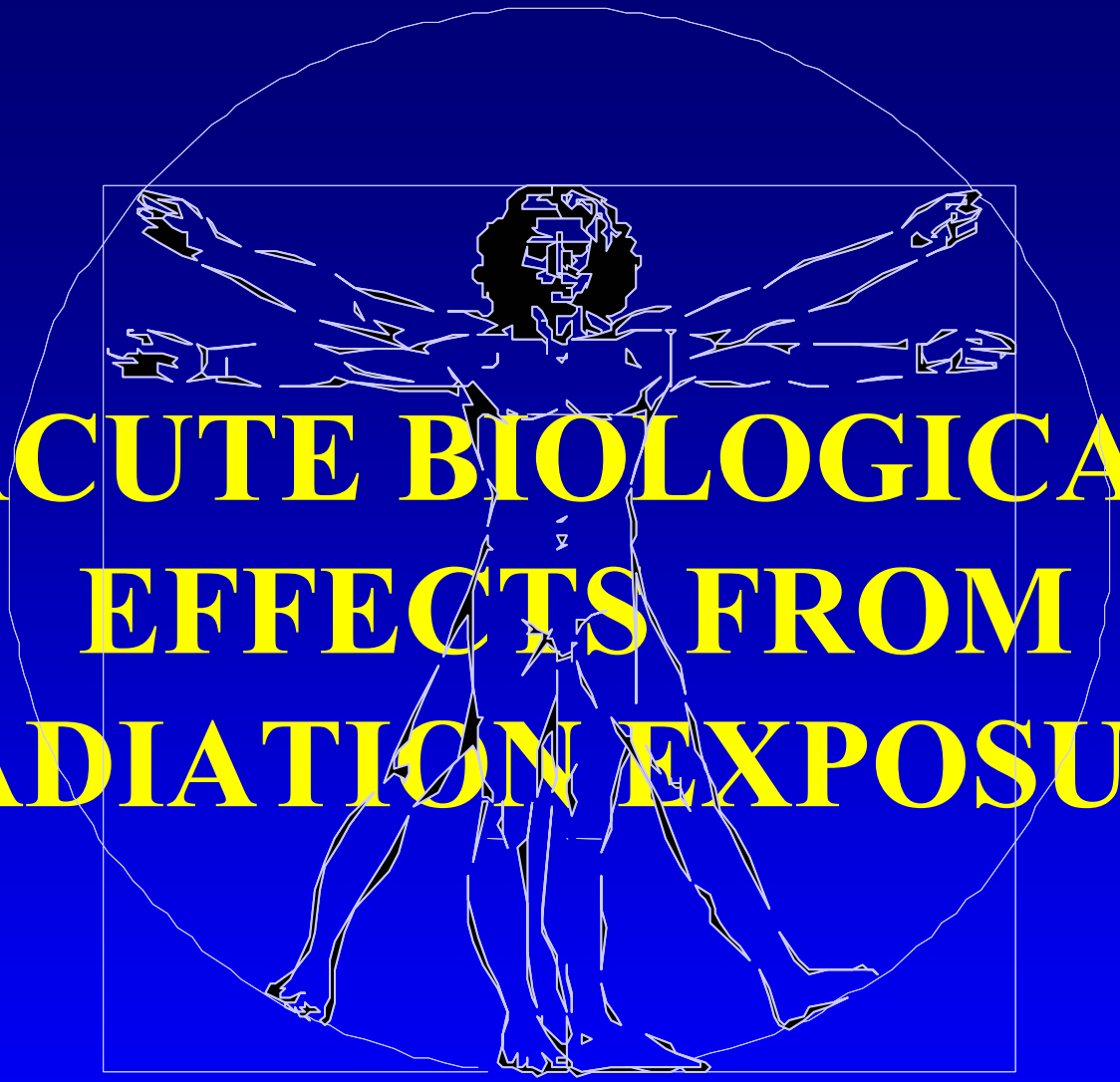
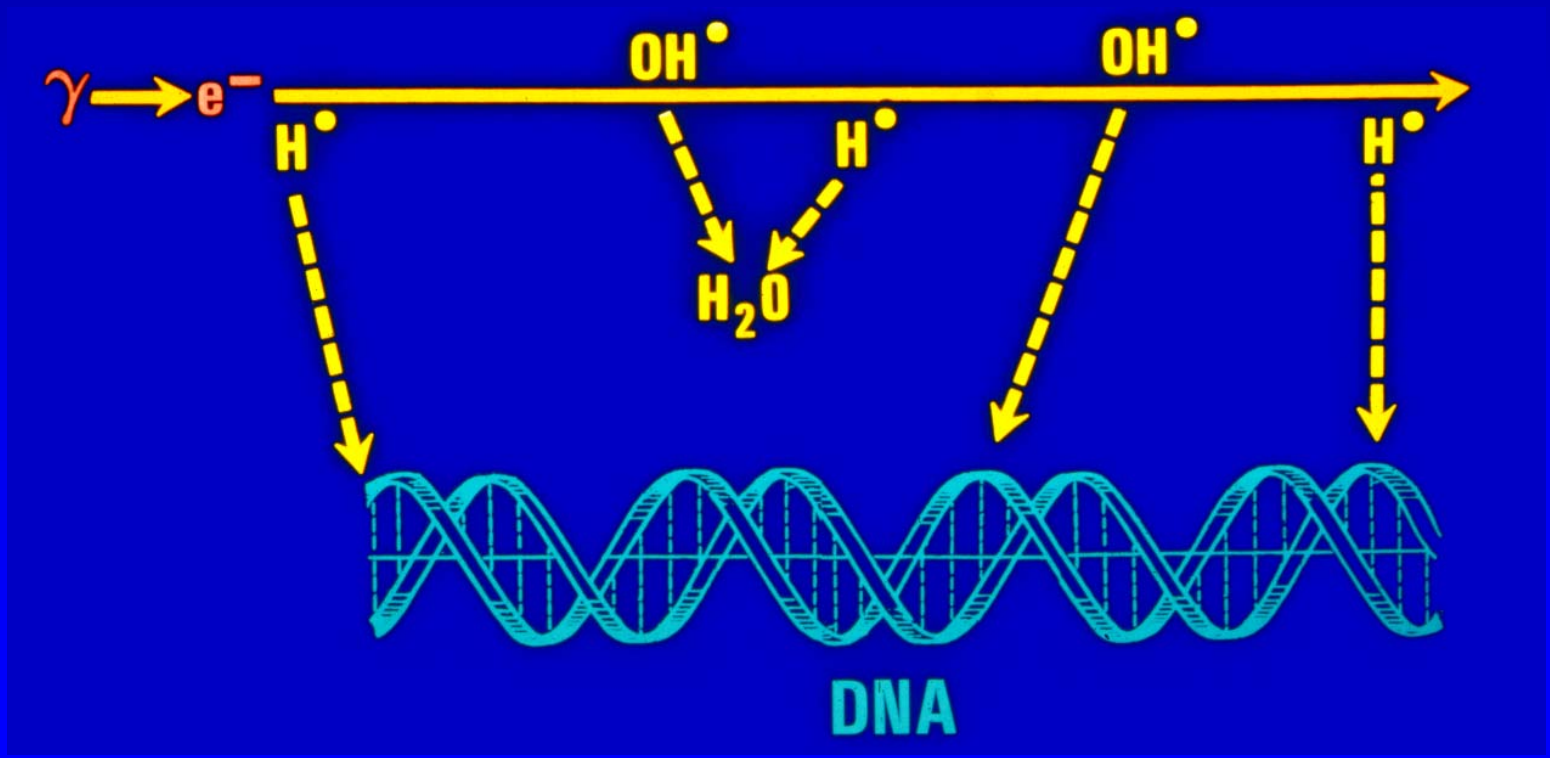
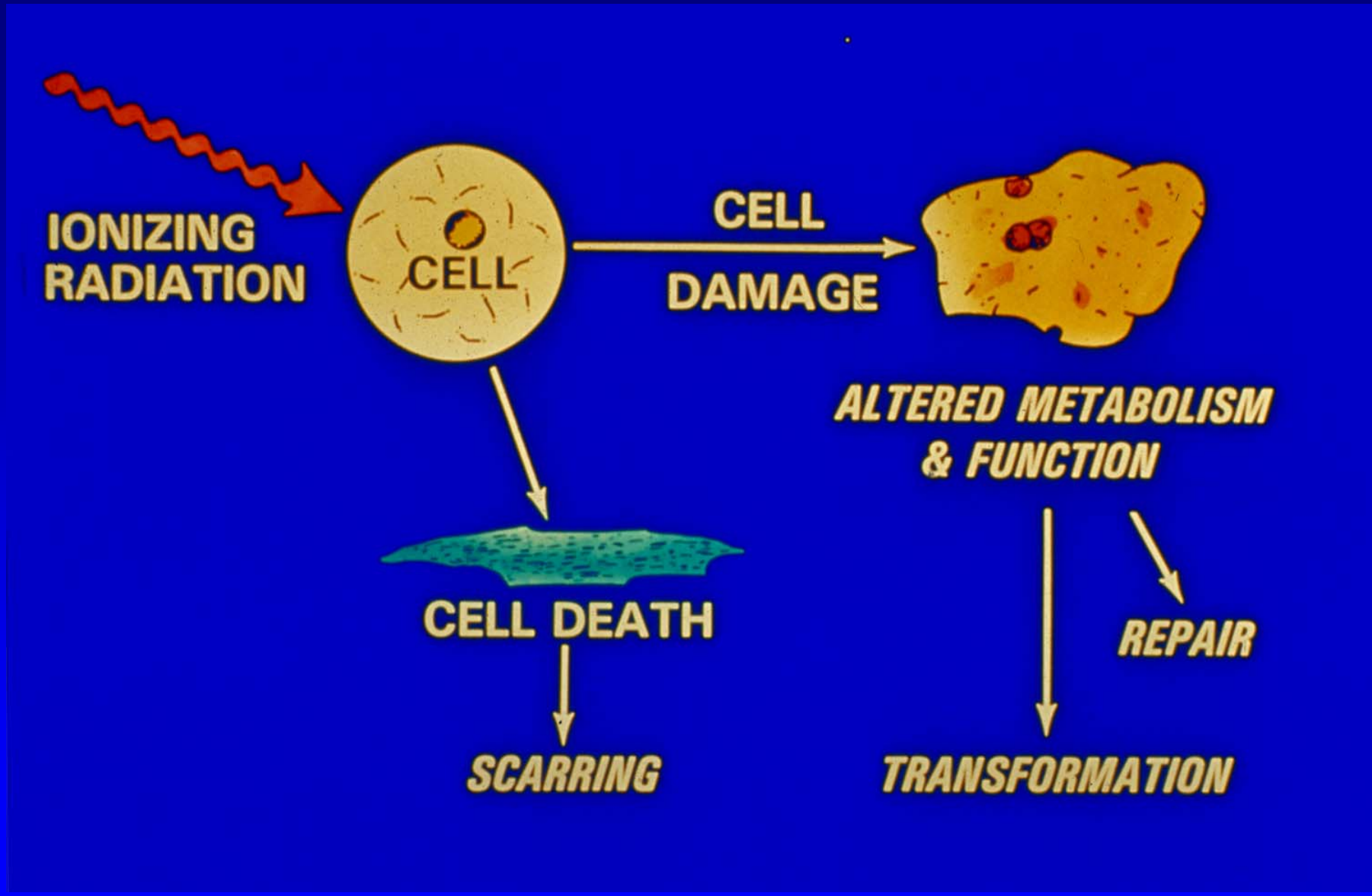


ACUTE BIOLOGICAL EFFECTS FROM RADIATION EXPOSURE

Dr. Jerrold T. Bushberg
Clinical Professor, Radiology
Director of Health Physics Programs
University of California, Davis

Initial Radiation Interactions



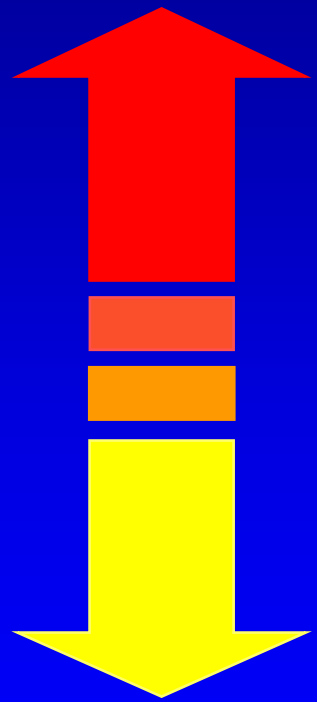

IONIZING
RADIATION
CELL
CELL
DAMAGE
ALTERED METABOLISM
& FUNCTION
CELL DEATH
REPAIR
SCARRING
TRANSFORMATION

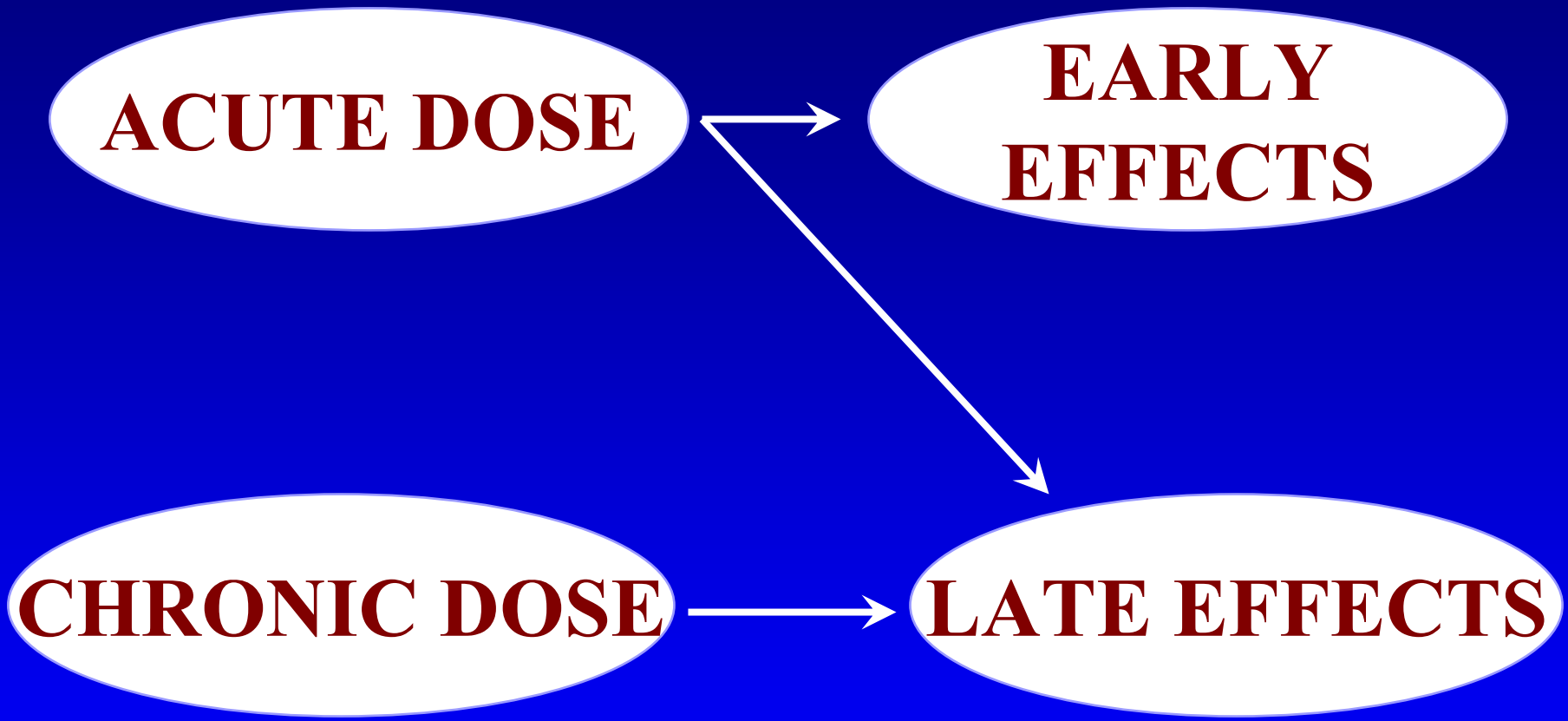
Law of Bergonie and Tribondeau (1906)

The radiosensitivity of a tissue is proportional to its reproductive capacity and inversely proportional to its degree of differentiation.

Sensitivity of Cells/Tissues

- White Blood Cells
- Bone Marrow
- Skin Cells
- GI Tract
- Nerve and Brain Cells

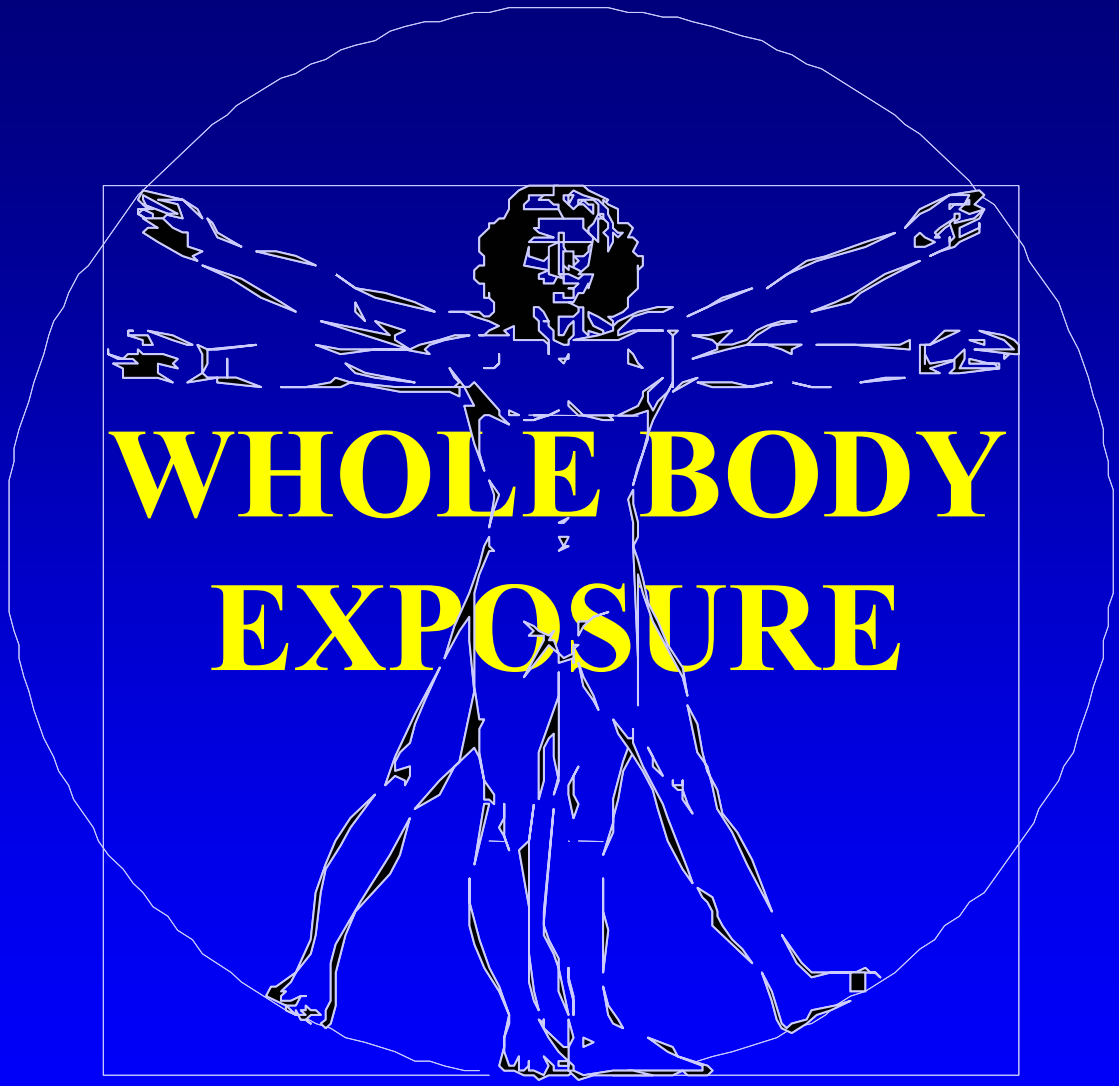



ACUTE DOSE
EARLY EFFECTS
CHRONIC DOSE
LATE EFFECTS

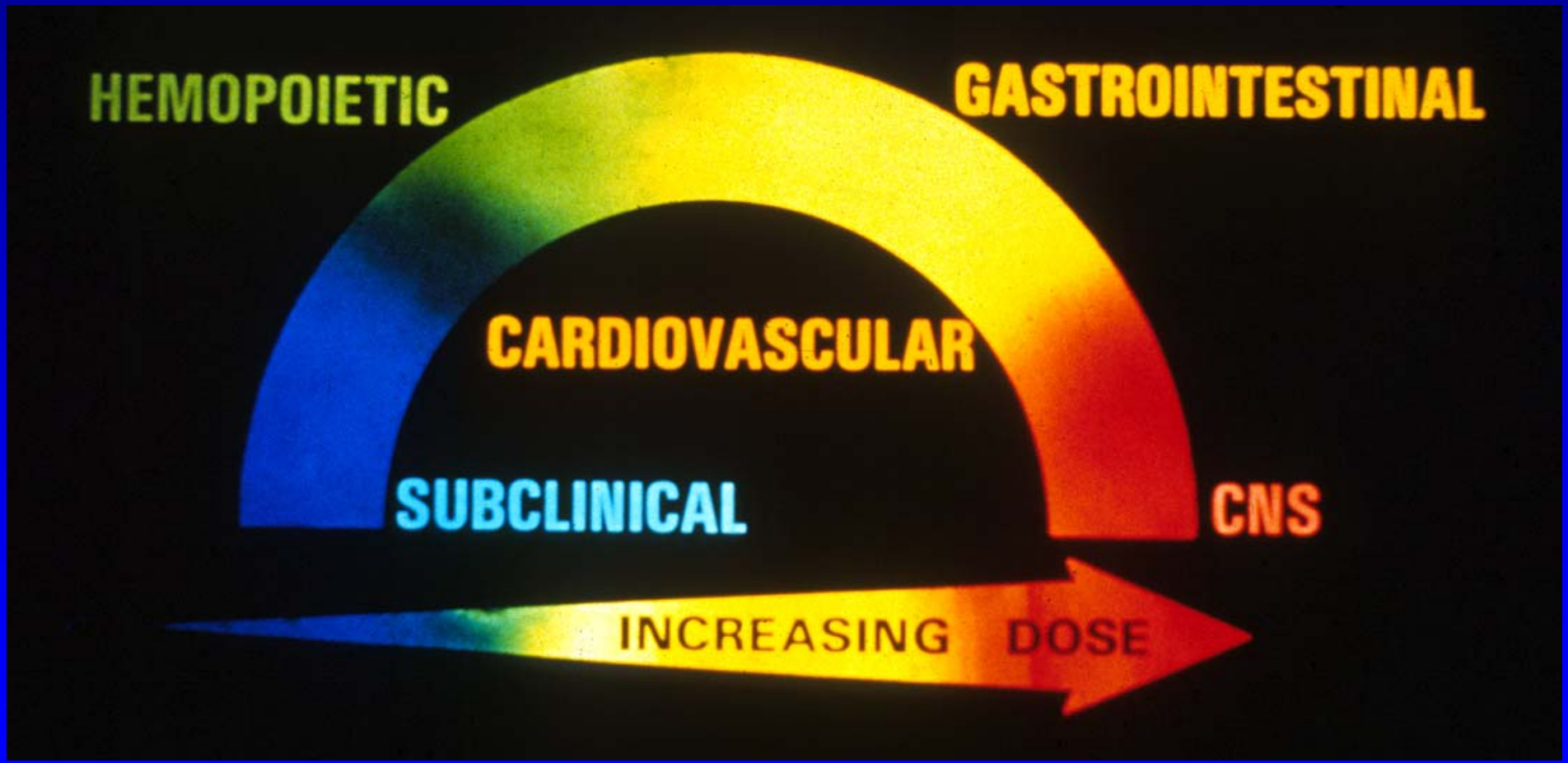
High Dose Acute Exposure

- **Dose delivered quickly (few hours)**
- **Effects appear quickly (days to weeks)**
- **Relatively high doses required [>1 Gy* (>100 rad)]**

* Gy = gray(SI unit)


WHOLE BODY
EXPOSURE

Acute Radiation Syndrome



Acute Radiation Syndrome

Stage

Initial or Prodromal

Latent Period

Manifest Illness

Recovery Stage

External Exposure and Early Clinical Symptoms

Dose In air	SX in 50%
120 rad	Anorexia
170 rad	Nausea
210 rad	Vomiting
240 rad	Diarrhea

Factors That Alter Response to Radiation Damage

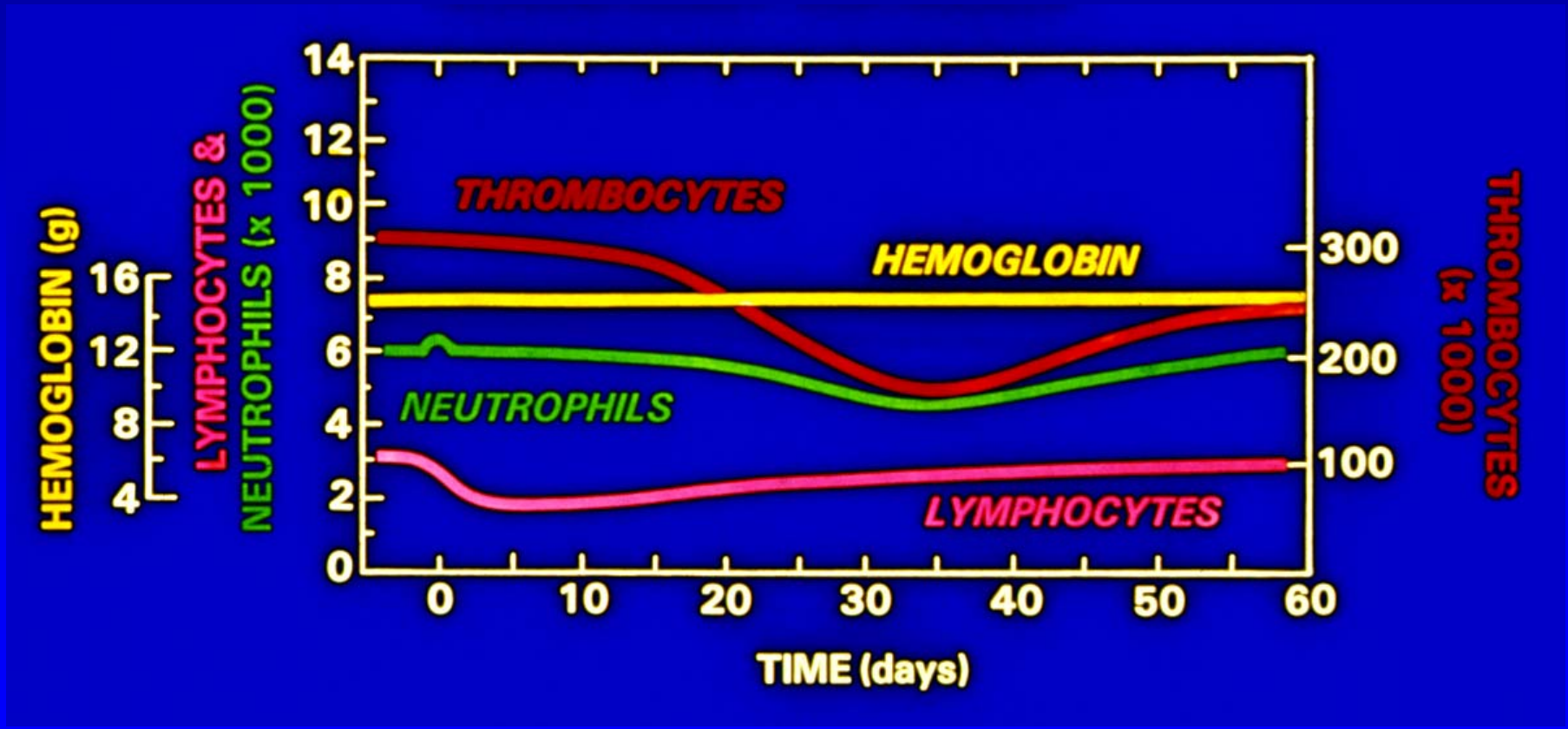
- Total Dose
- Dose Rate
- Portion of the Body Exposed
- Uniformity of Exposure
- Age of the Victim
- State of Health
- Availability of Treatment

Hematopoietic Syndrome

100-800 rad

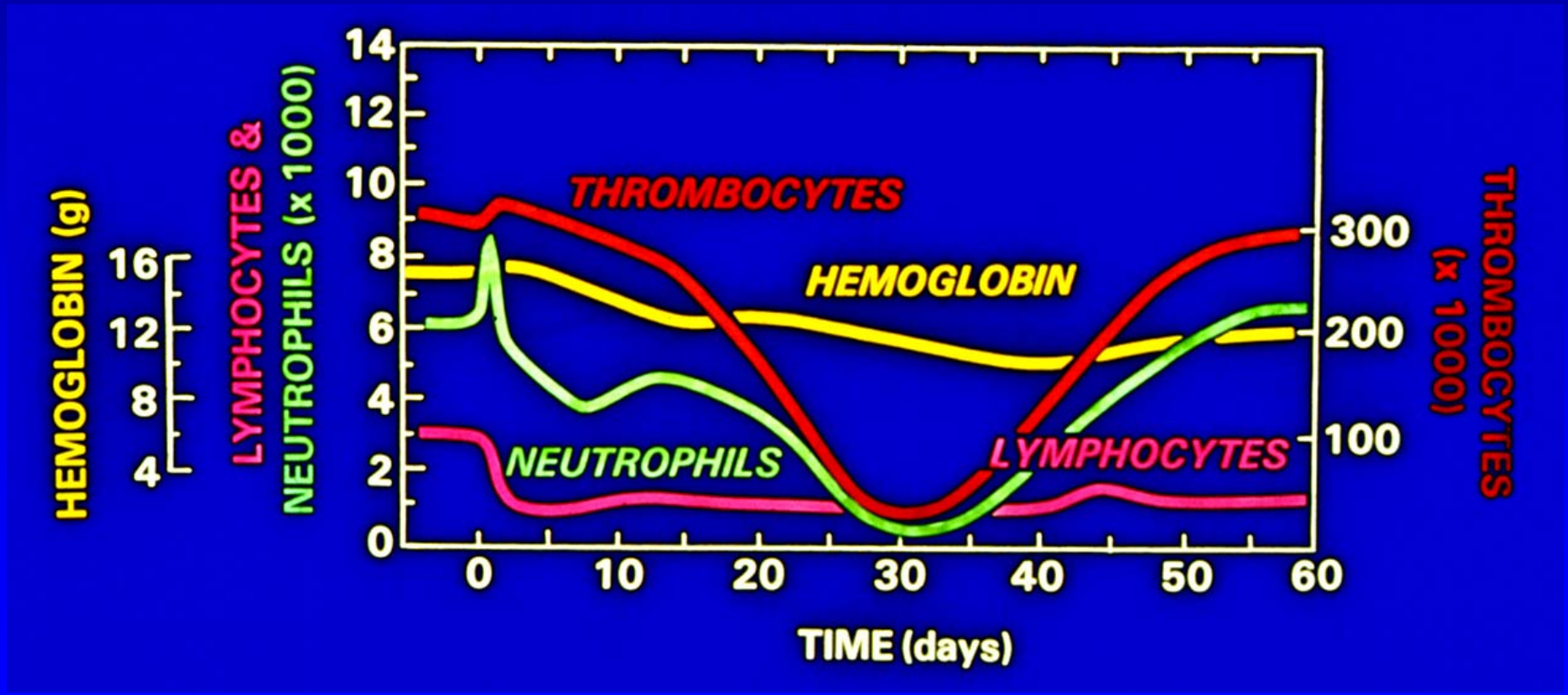
Hematological Response to 100 rad

Whole Body Exposure

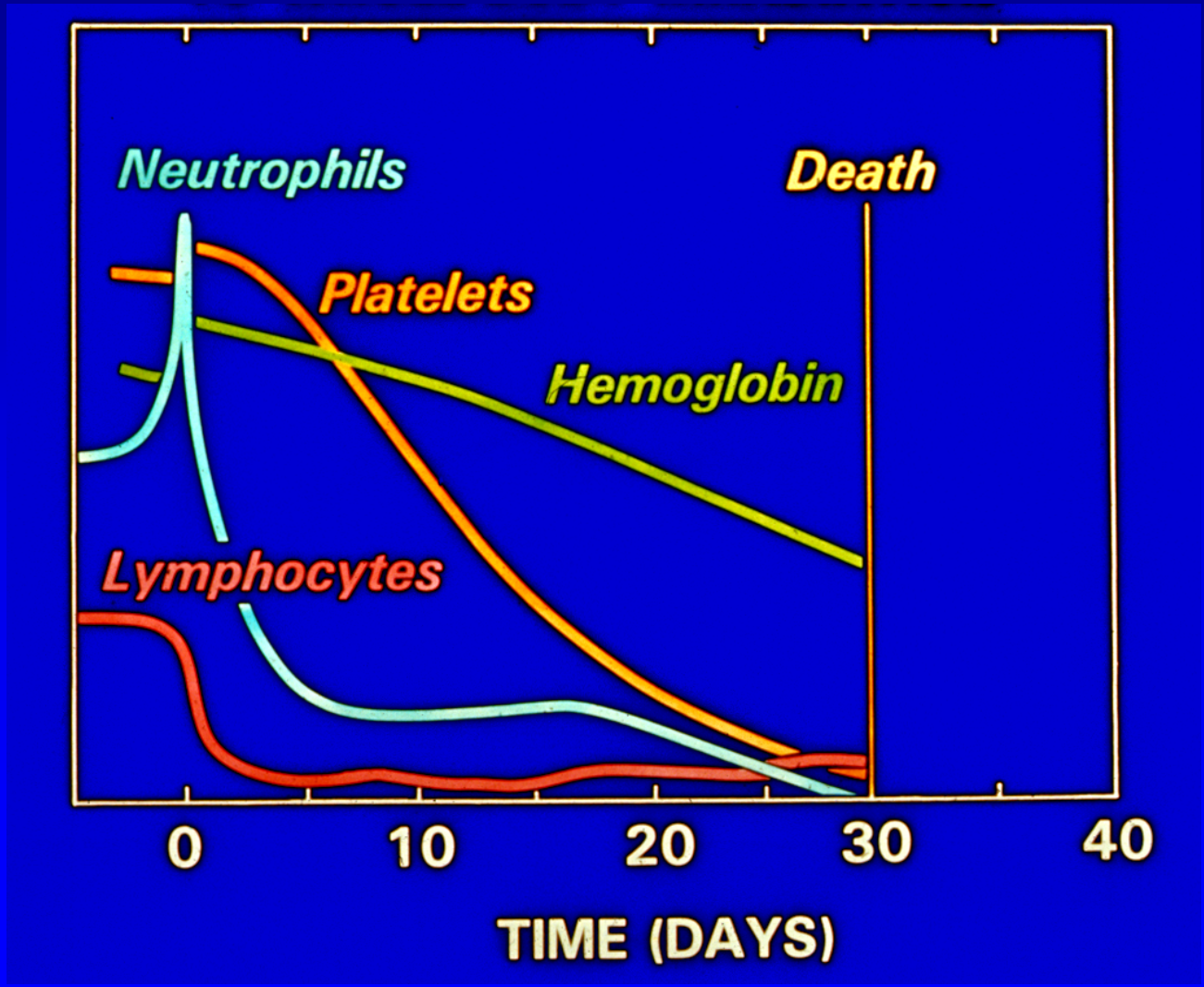


Hematological Response to 300 rad

Whole Body Exposure



Hematological Response
to Whole Body Irradiation



Bone Marrow Syndrome

- Leukopenia
- Anemia
- Thrombocytopenia

Secondary

- Hemorrhage
- Infection

Gastrointestinal Syndrome

800-3000 rad

Gastrointestinal Syndrome

Prodromal Period

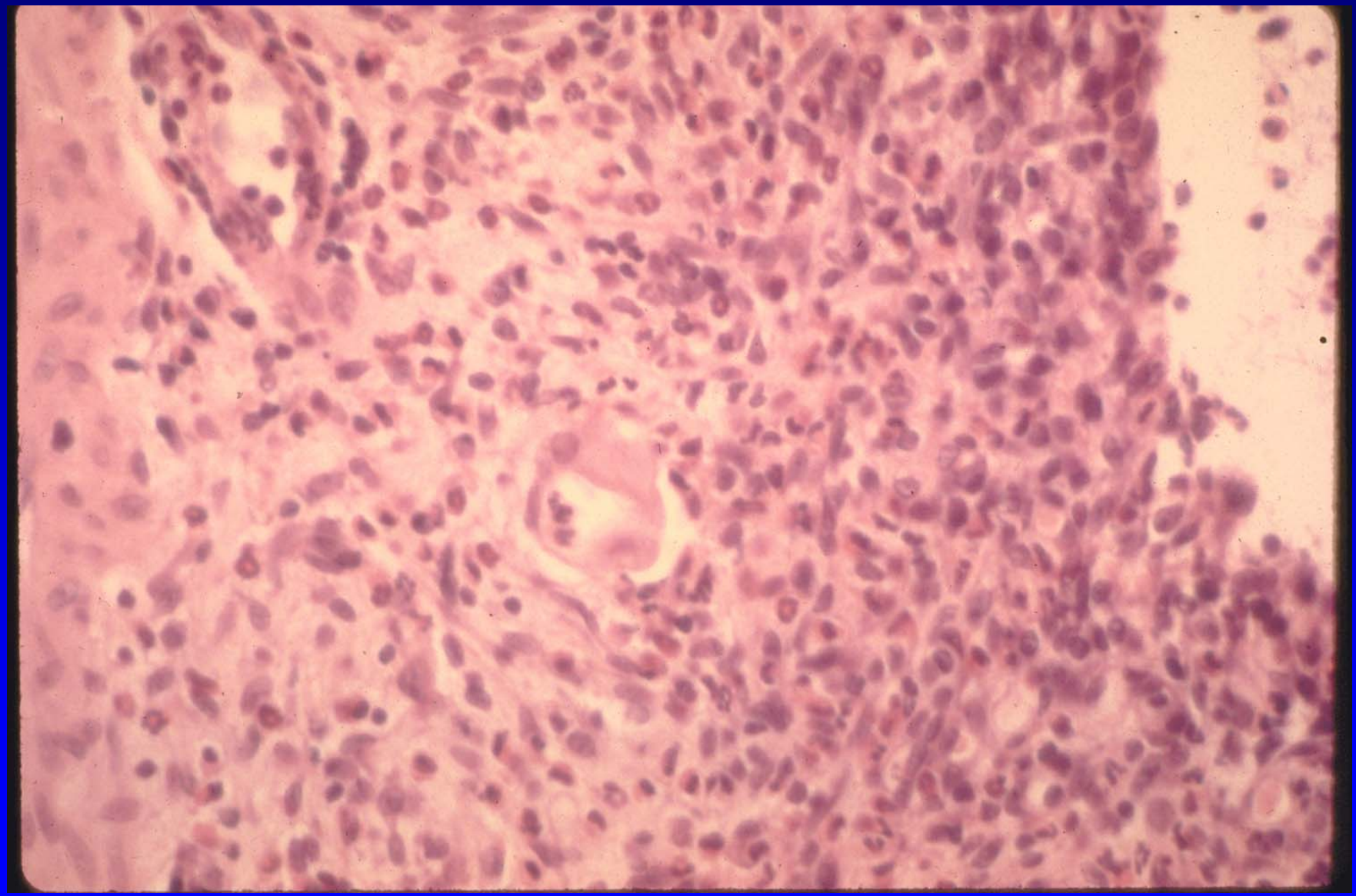
Severe nausea, vomiting and occasionally watery diarrhea and cramps, within hours after exposure.

Gastrointestinal Syndrome

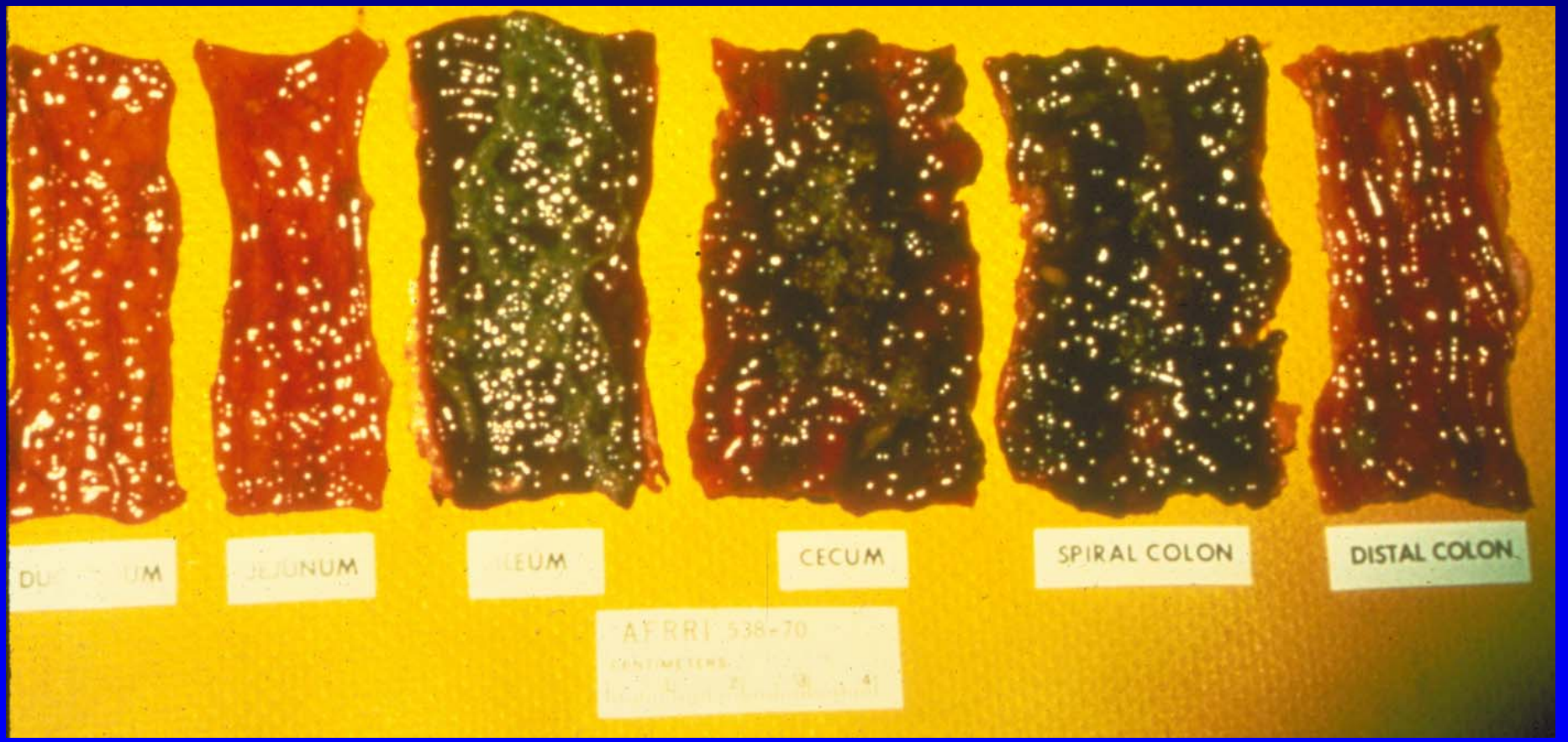
Overt Clinical Picture

Return of severe diarrhea, vomiting and diarrhea with fever.

Progression to bloody diarrhea, shock and death.




DUODENUM
JEJUNUM
ILEUM
CECUM
SPIRAL COLON
DISTAL COLON
AFRRI CONTROL
CENTIMETERS
1
2
3
4


JEJUNUM
CECUM
SPIRAL COLON
DISTAL COLON
AFRRI 538-70

Systemic Effects of GI Syndrome

- Malabsorption
  - Malnutrition
- Paralytic Ileus
  - Vomiting
  - Abdominal Distension
- Fluid and Electrolyte Shifts
  - Dehydration
  - Acute Renal Failure
  - Cardiovascular Collapse
- GI Bleeding
  - Anemia
- Sepsis

Cardiovascular/Central Nervous System Syndrome

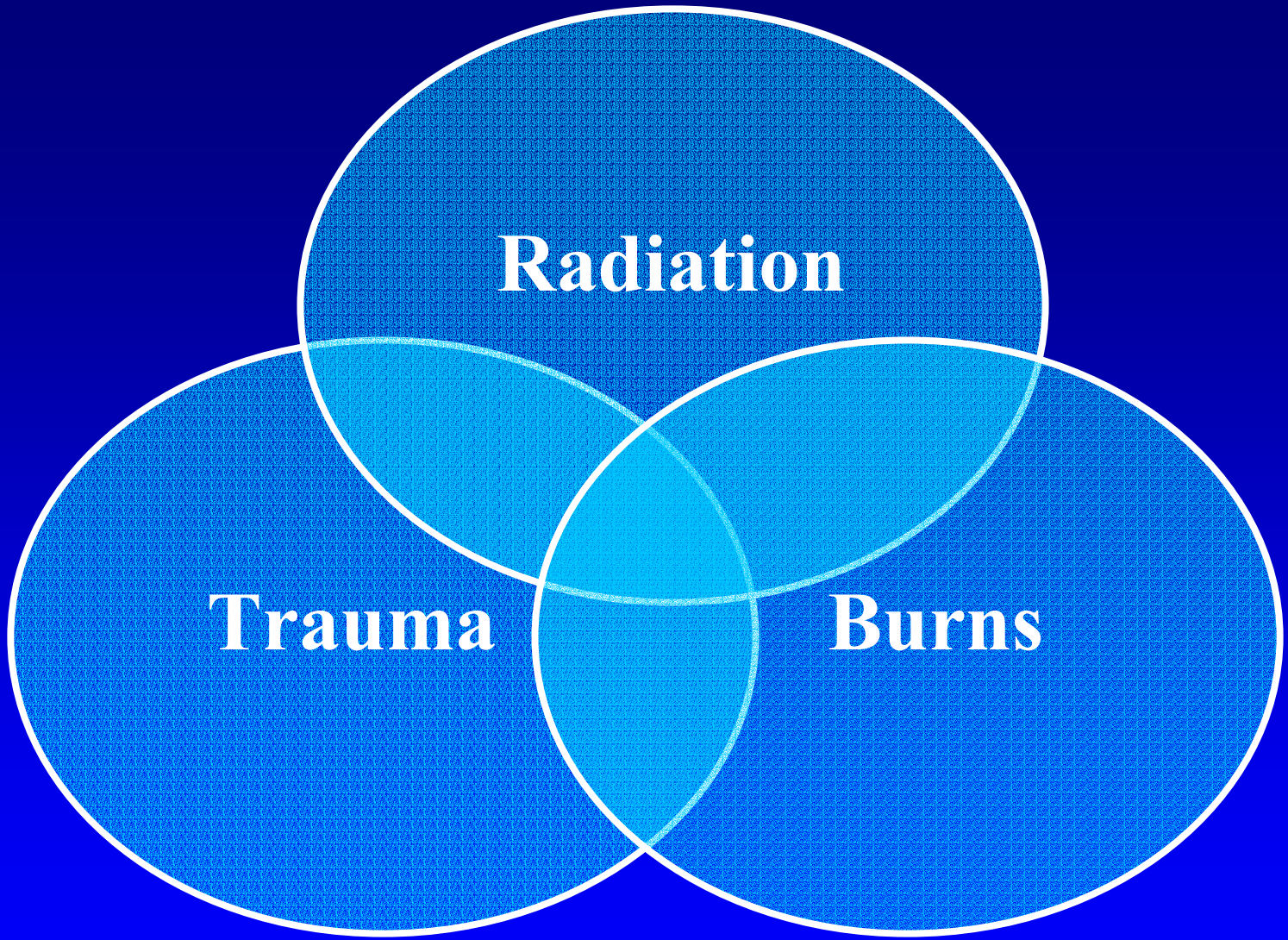
3000 rad and above

Cardiovascular/Central Nervous System Symptoms

- Vomiting and diarrhea within minutes
- Confusion and disorientation
- Severe hypotension
- Edema
- Hyperpyrexia
- Fatal within 24-48 hours

Acute Radiation Syndrome (Summary)

Dose (rads)	Effects
<50	Clinical threshold (drop in lymphocyte count)
~100	Threshold for Prodrome
~350	~50% die within 60 days (with minimal supportive care)
~500	~50% die within 60 days (with supportive medical care)
>1,000	~100% die within 30 days


Radiation
Trauma
Burns

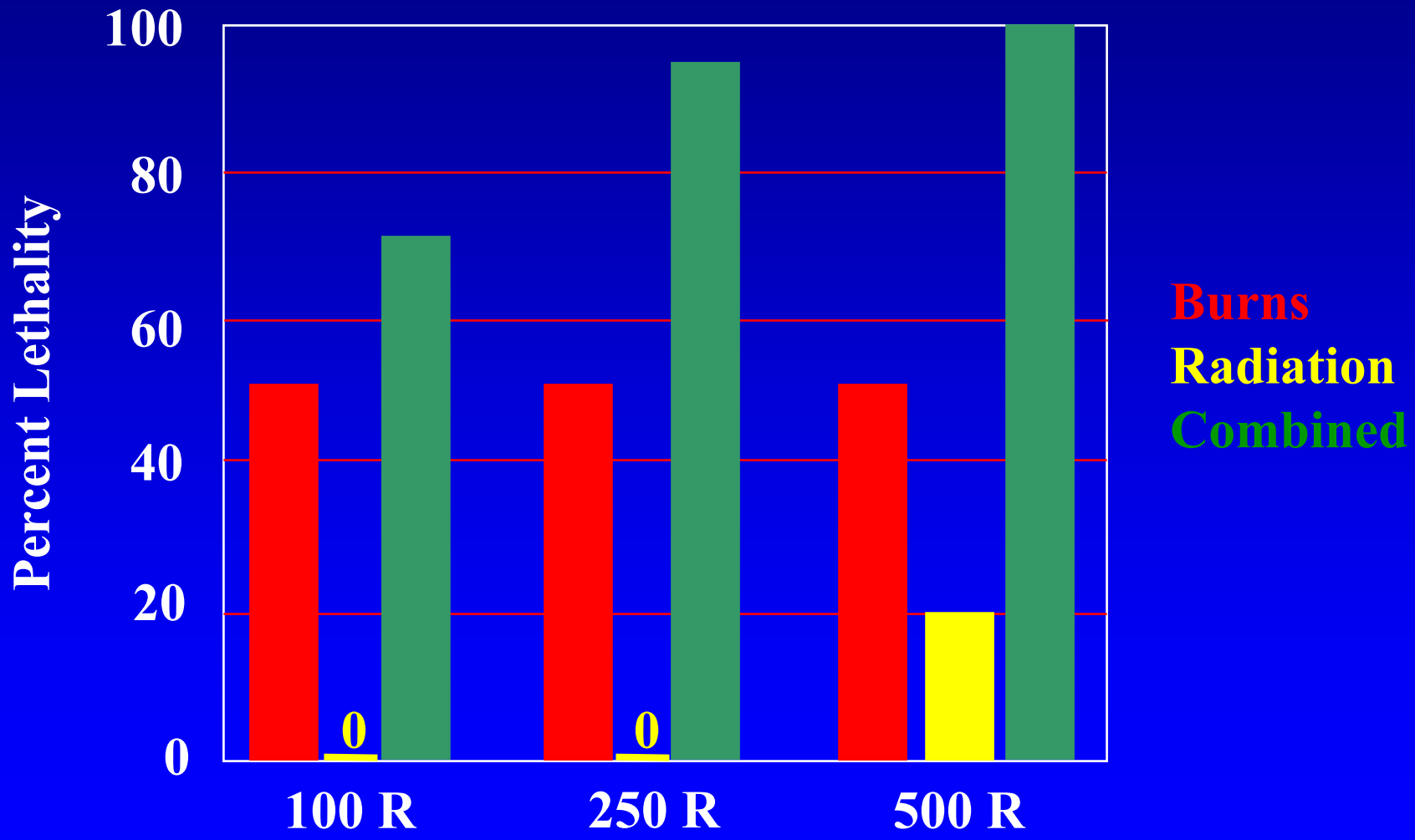
Prognosis for almost all combined injuries is worse than for irradiation injury alone.

BURNS

AND

RADIATION

Combined Effects of Simultaneous Whole Body Irradiation and Burns on Rats

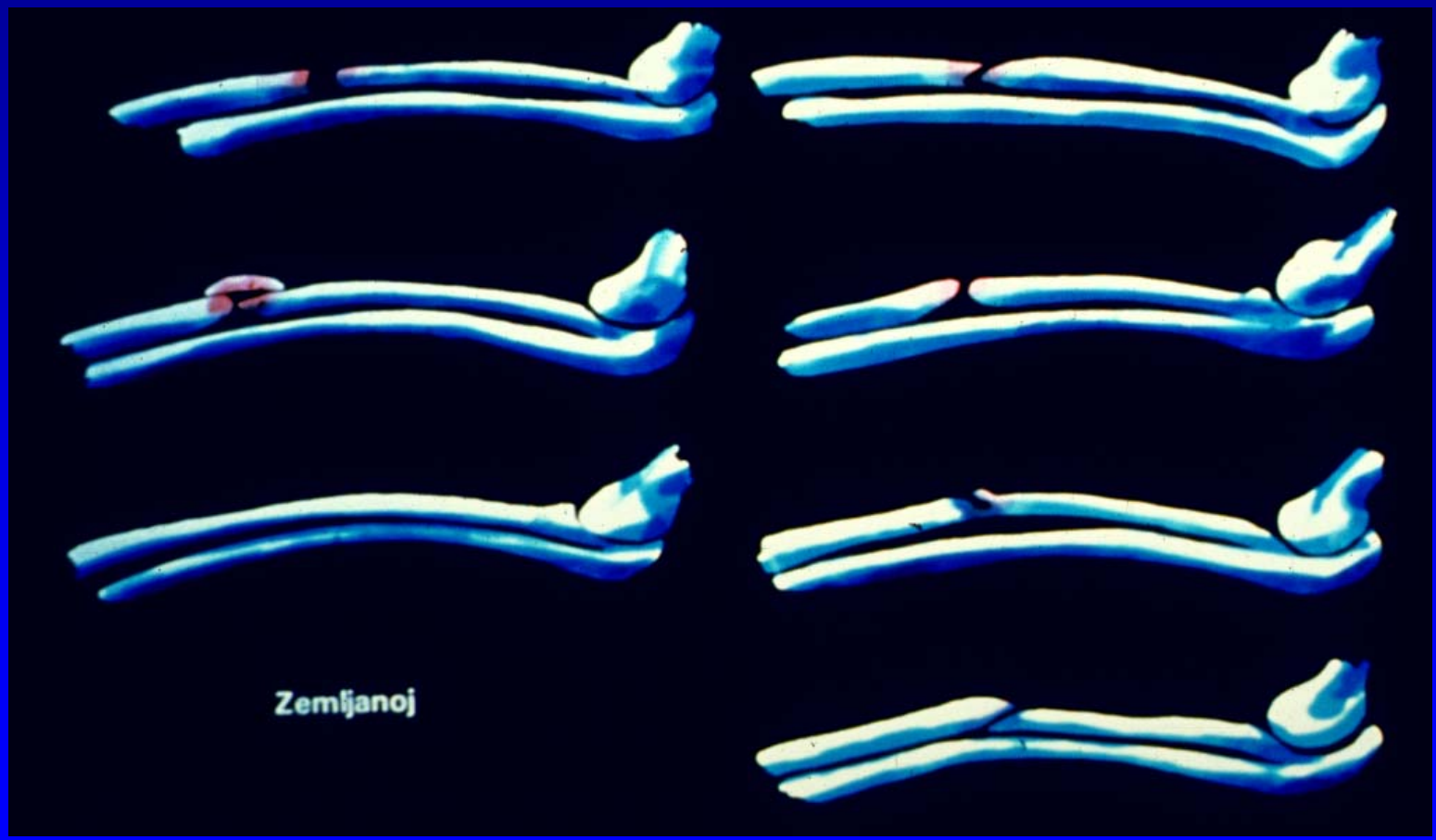


WOUNDS

AND

RADIATION

Healing of Rabbit Fractures




CHERNOBYL

Triage of Radiation Injuries

Symptoms	Unlikely	Probable	Severe
Nausea	—	++	+++
Vomiting	—	+	+++
Diarrhea	—	+/ —	+/ — to +++
Hyperthermia	—	+/ —	+ to +++
Erythema	—	—	— to ++
Hypotension	—	—	+ to ++
CNS Dysfunction	—	—	— to ++

Chernobyl Nuclear Power Station Acute Radiation Syndrome

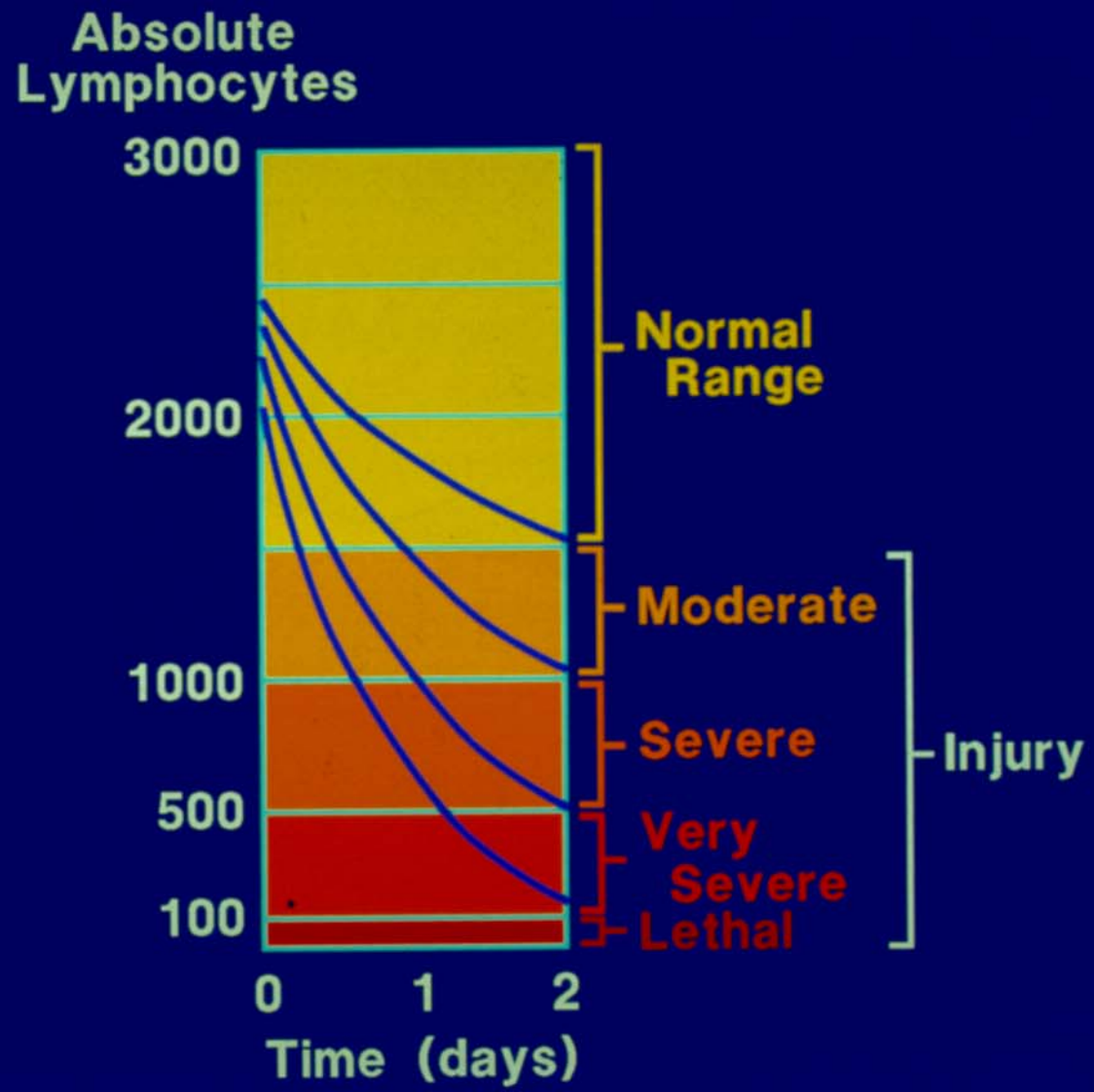
Dose (rem)	Vomiting (hours)	Number of Patients	Number of Deaths
100-200	>2	139	0
200-400	1-2	53	1
400-600	0.5-1	23	7
>600	<0.5	22	21
		237	29

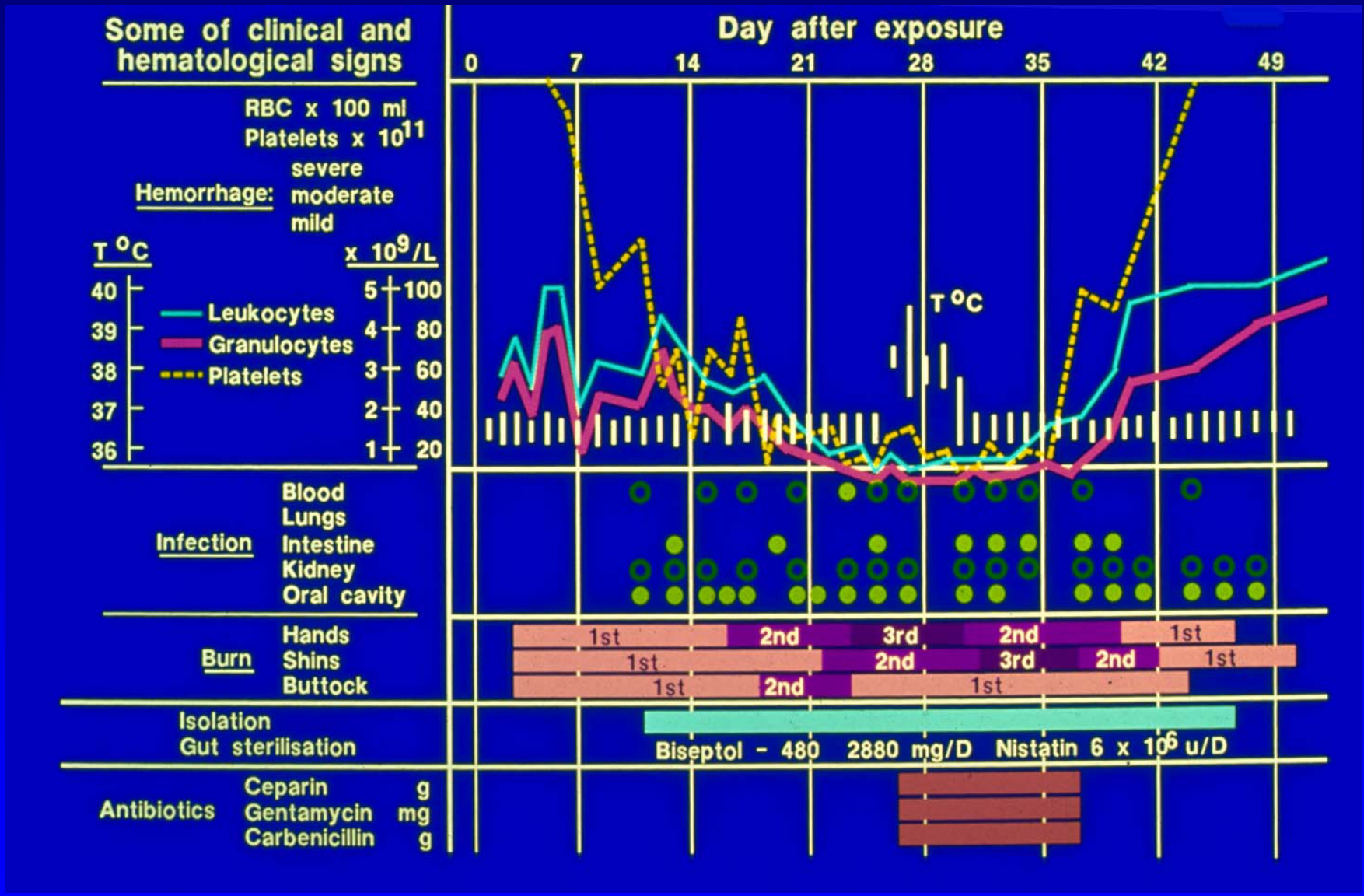
Relationship Between

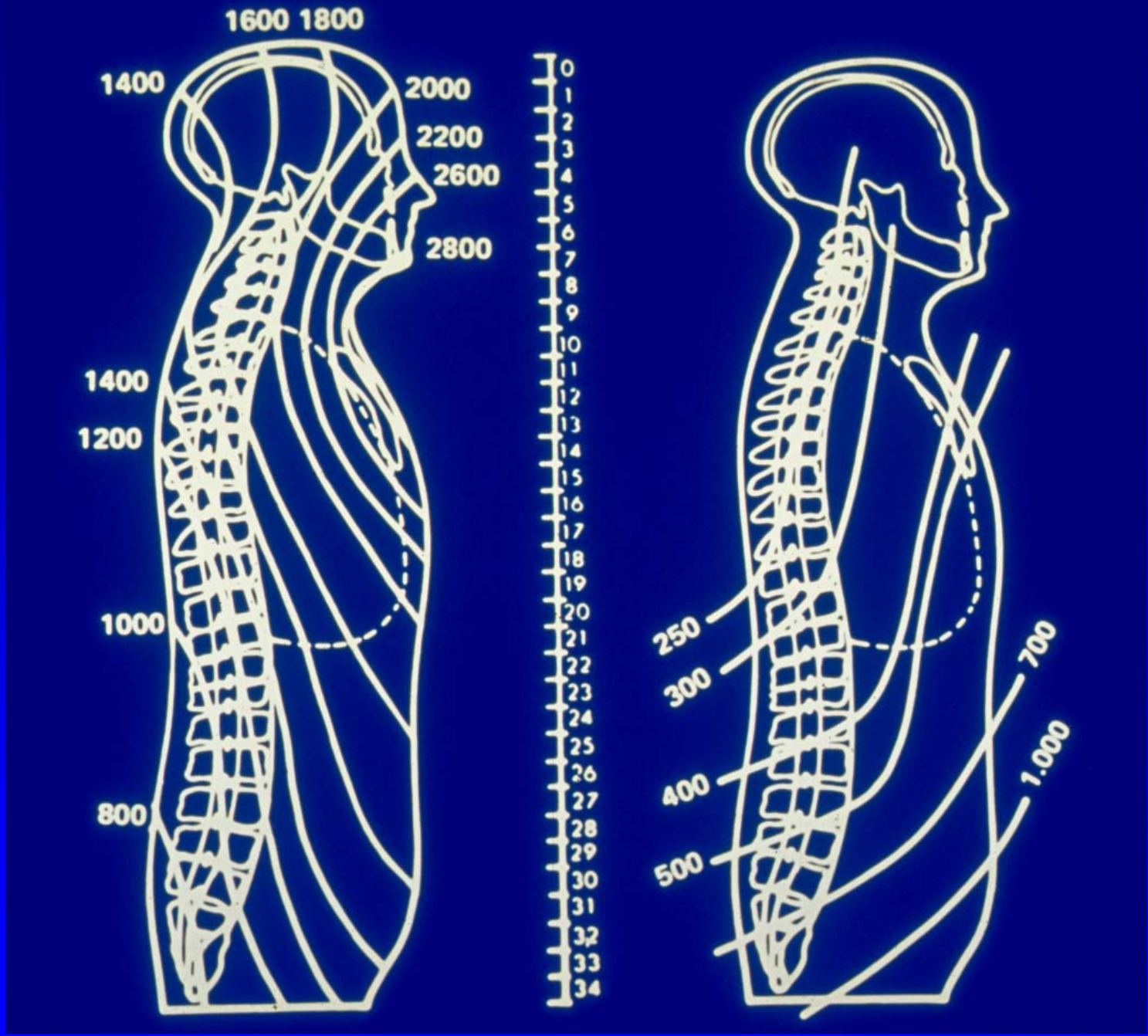
Early Changes in Peripheral Blood Lymphocyte Counts

and

Degree of Radiation Injury




Some of clinical and hematological signs
Day after exposure
0
7
14
21
28
35
42
49
RBC x 100 ml
Platelets x 10^{11}
Hemorrhage:
severe
moderate
mild
T °C
x 10^9/L
40
39
38
37
36
5
4
3
2
1
100
80
60
40
20
Leukocytes
Granulocytes
Platelets
T °C
Infection
Blood
Lungs
Intestine
Kidney
Oral cavity
Burn
Hands
Shins
Buttock
1st
2nd
3rd
2nd
1st
1st
2nd
3rd
2nd
1st
1st
2nd
1st
Isolation
Gut sterilisation
Biseptol - 480 2880 mg/D Nistatin 6 x 10^6 u/D
Antibiotics
Ceparin g
Gentamycin mg
Carbenicillin g


1600 1800
1400
2000
2200
2600
2800
1400
1200
1000
800
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34
250
300
400
500
700
1.000

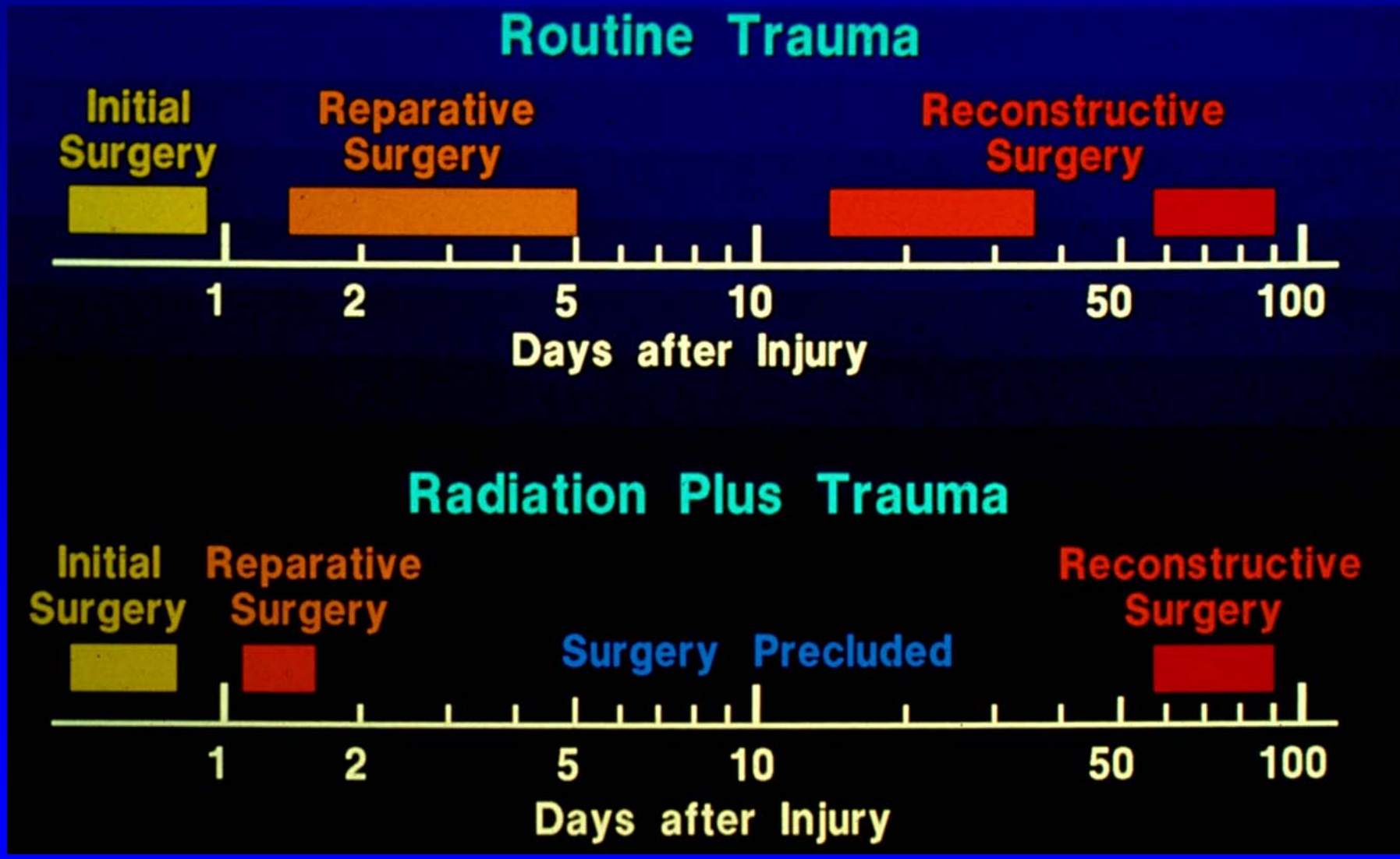
Bone Marrow Transplantation Chernobyl Experience

- 22 individuals with a radiation dose of greater than 600 rad.
- 13 received allogenic transplantations
- 6 received fetal liver extracts
- 21/22 died
- One survivor rejected allogenic transplant

Surgery in Combined Injuries

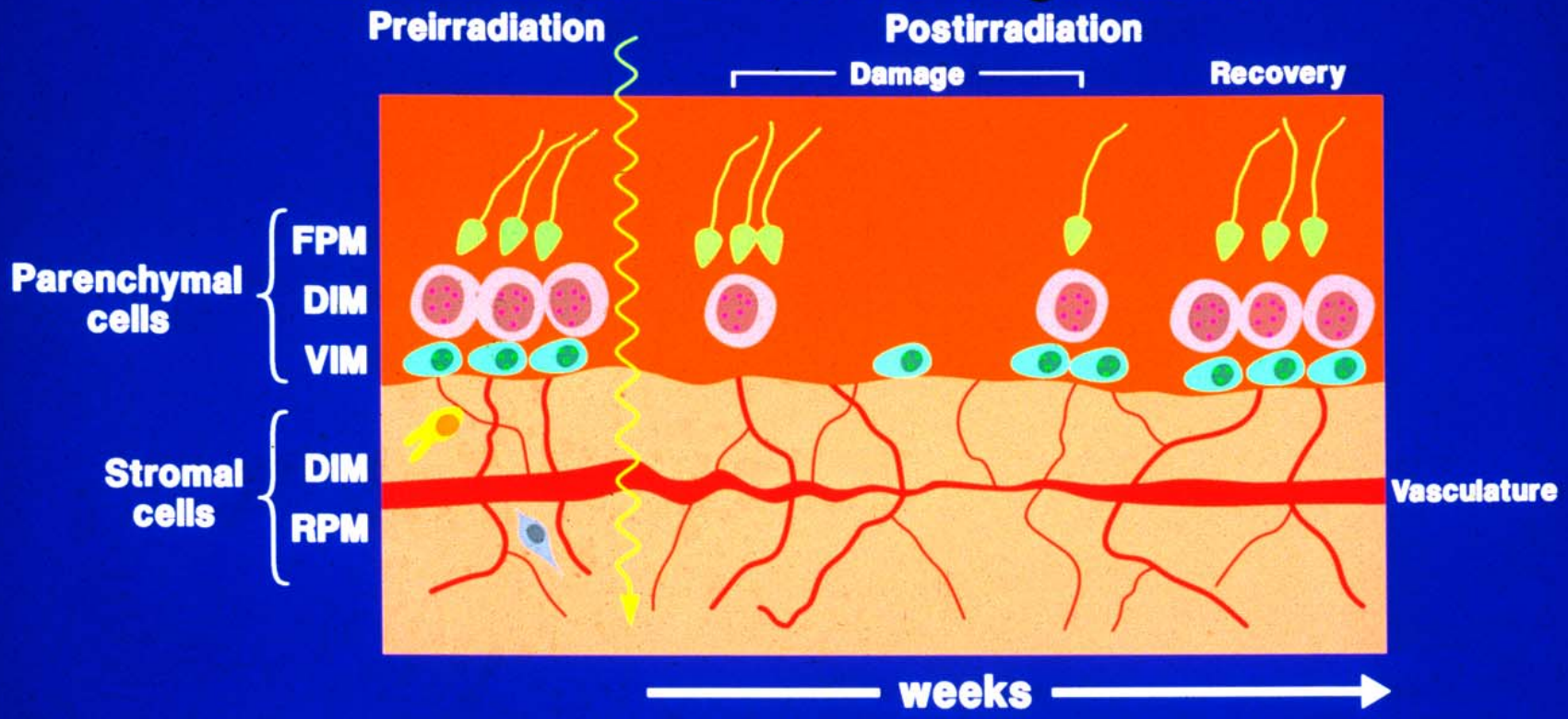
WTT70

Timing of Surgical Management of Combined Injuries



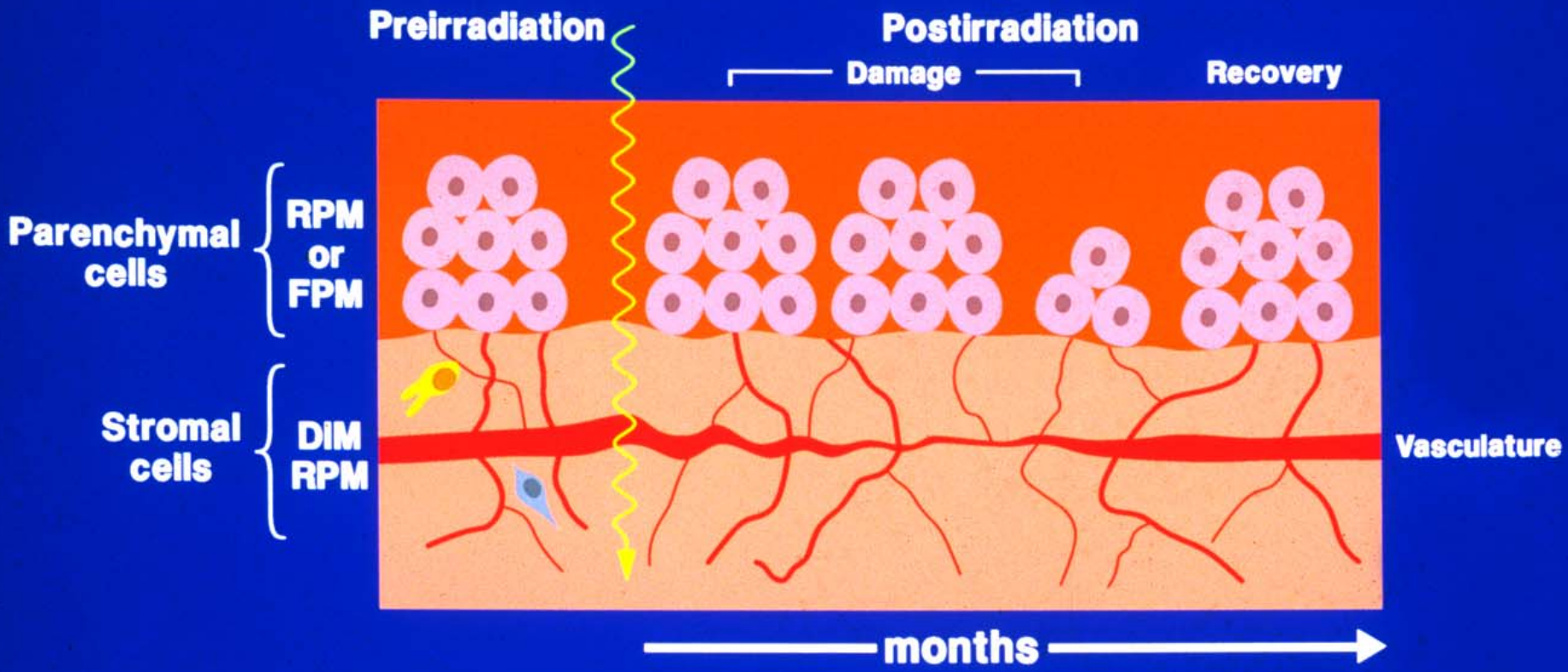
LOCAL RADIATION INJURY

Radiosensitive Tissue (e.g. Testis)



- Radiosensitivity: Parenchymal > Stromal
- Stromal damage not the primary contributor to organ damage

Radioresistant Tissue (e.g. muscle)



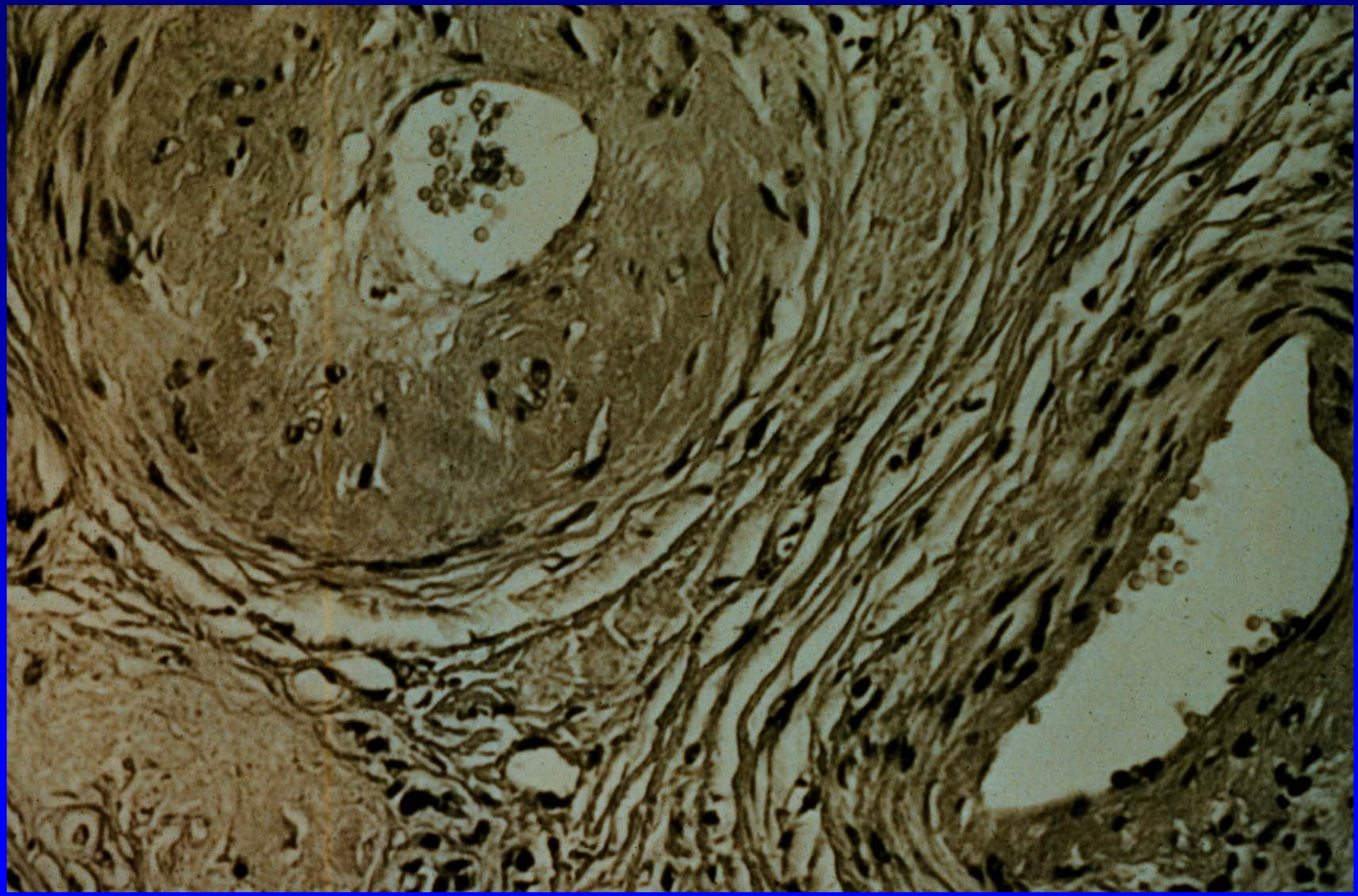
- Radiosensitivity: Stromal > Parenchymal
- Damage to parenchymal cell is indirect via vascular compromise

Radiation Induced Skin Injuries

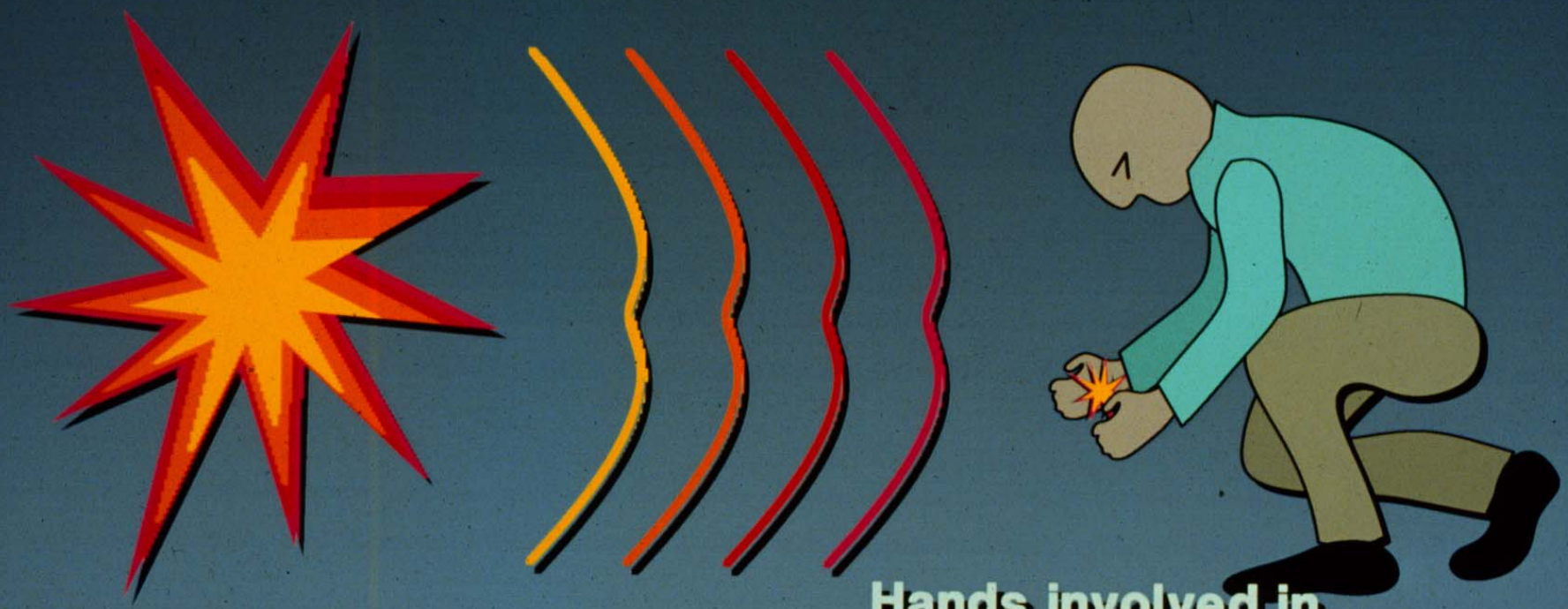
Effect	Typical Dose (rad)	Latent Period
Early Transient Erythema	200	1-2 hrs.
Temporary Epilation	300	3-4 wks.
Main Erythema	600	2-3 wks.
Permanent Epilation	700	1-3 wks.
Dry Desquamation	1,000-1,500	4 wks.
Moist Desquamation	1,500-2,000	2-4 wks.
Ulceration	2,000	> 6 wks.
Dermal Necrosis	> 2,500	2-10 wks.

Dose Fractionation Effect (rads)

Effect	Single Dose	3 doses in 3 days
Erythema	1,000	1,490
Dry Desquamation	1,600	2,700
Necrosis	3,000	4,400



LOCAL RADIATION EXPOSURE



Hands involved in more than 90% of cases

Four Extremity Radiation Necrosis: Surgical Management

- 39 YO male worked for approximately 20 minutes on the cooling system in the target area of a van de Graaf accelerator.
- Extremity dose approximately 6,000 rads.

Arch Surg 100:729-734

Erythema of right hand, fourth postaccident day.

Bullae formation, 17th postaccident day.

Desquamation with underlying granulation tissue, 35th postaccident day.

Pyocyaneus infection and early gangrene, 3 ½ months after accident.

Gangrene and pyocyaneus infection of thumb, 5 months after accident.

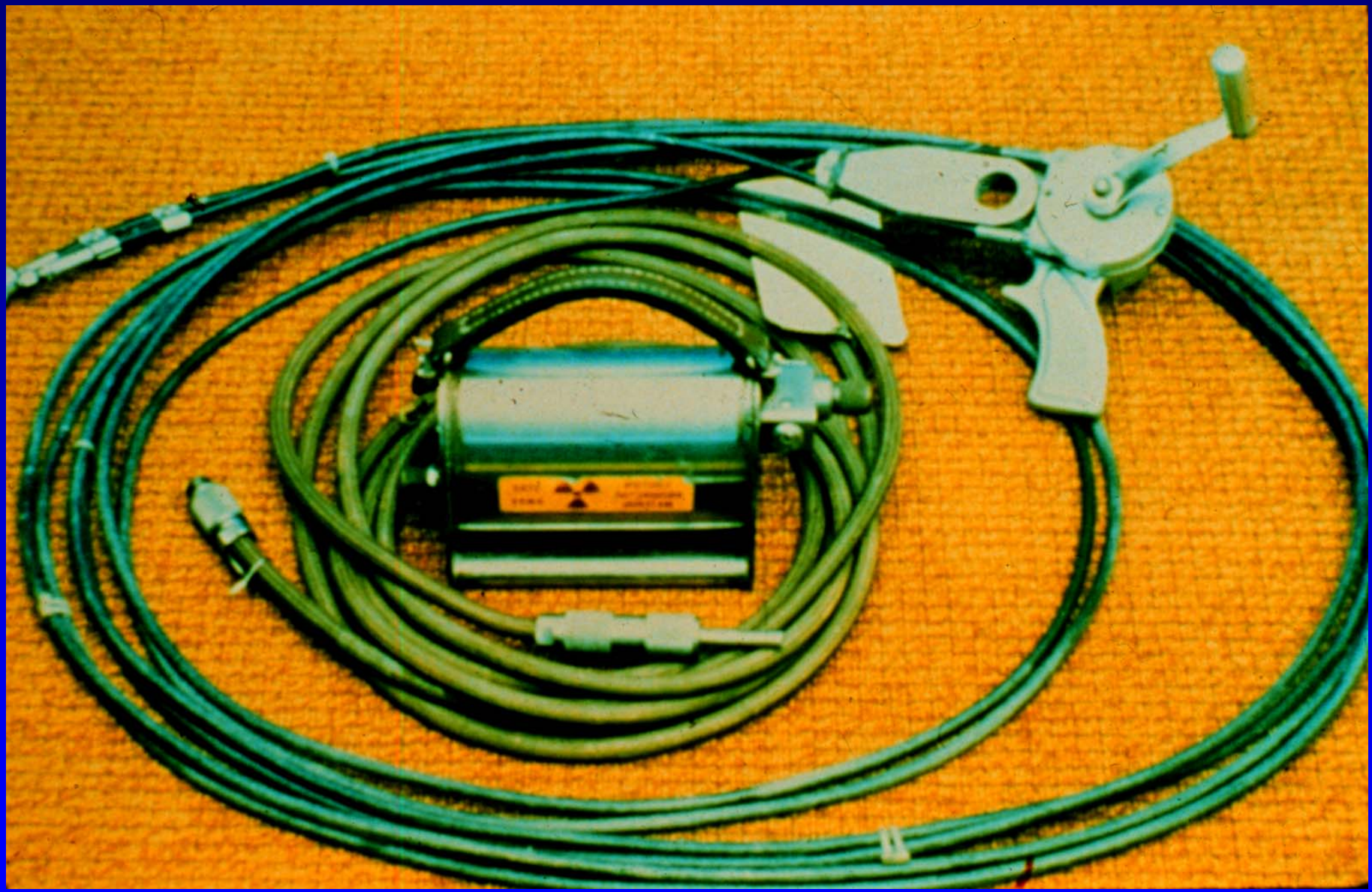
Hyperpigmentation and poor healing of right wrist amputation stump, 7 months after accident.

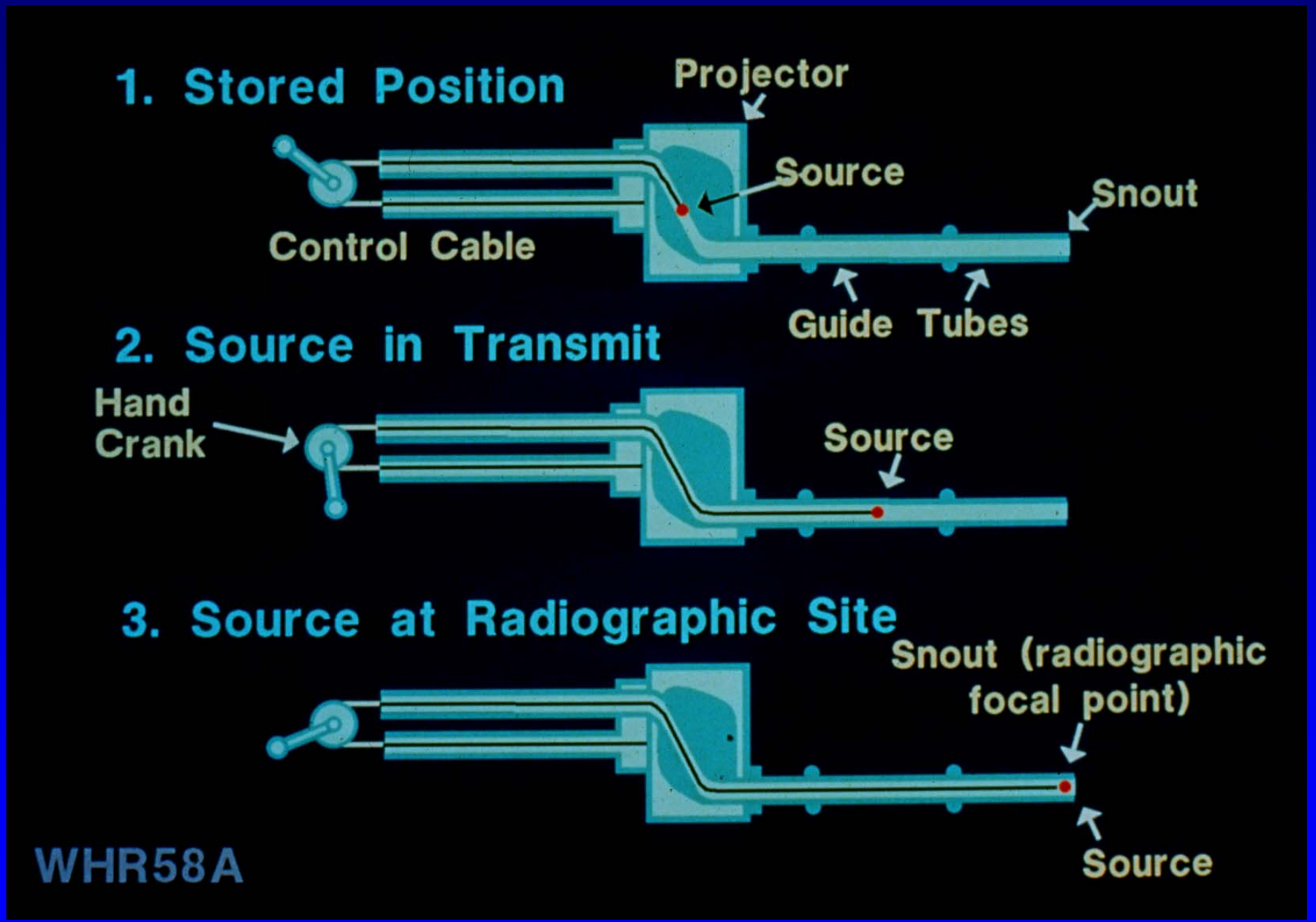
Ir-192 Accident Dosimetry Data

- Source:
  ^{192}Ir, 30 Ci (high energy betas & 300-600 keV gamma)
- Exposure rate:
  2,250 R/min at 1 cm

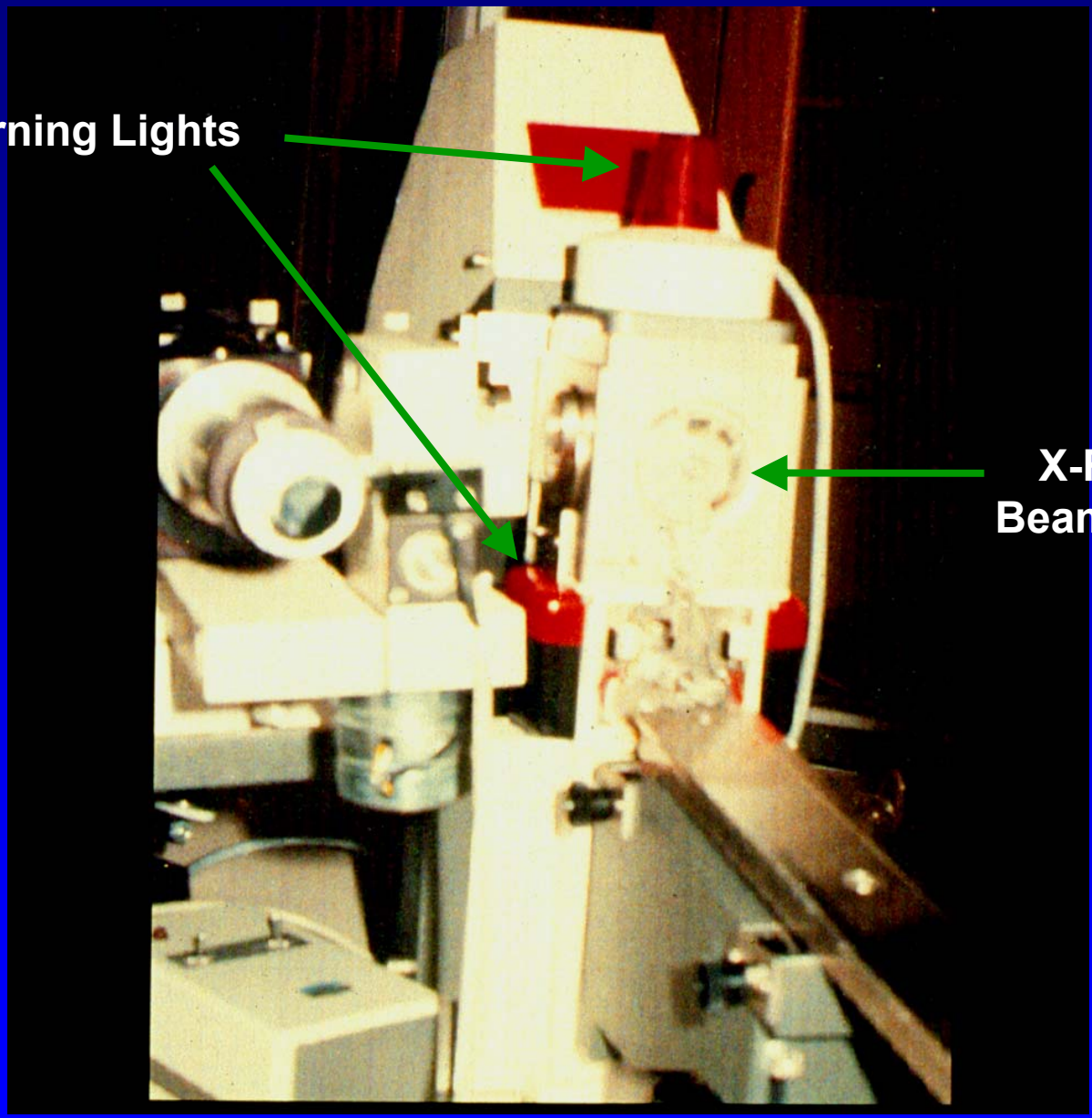
Depth Dose in Tissue (rad/45 min)

	Source Distance From Skin (cm)	
Depth (cm)	**0 cm**	**1 cm**
1	**52,000**	**16,000**
2	**19,000**	**9,000**
3	**5,200**	**3,400**
4	**1,800**	**1,300**




1. Stored Position
Projector
Source
Snout
Control Cable
Guide Tubes
2. Source in Transmit
Hand Crank
Source
3. Source at Radiographic Site
Snout (radiographic focal point)
Source
WHR58A

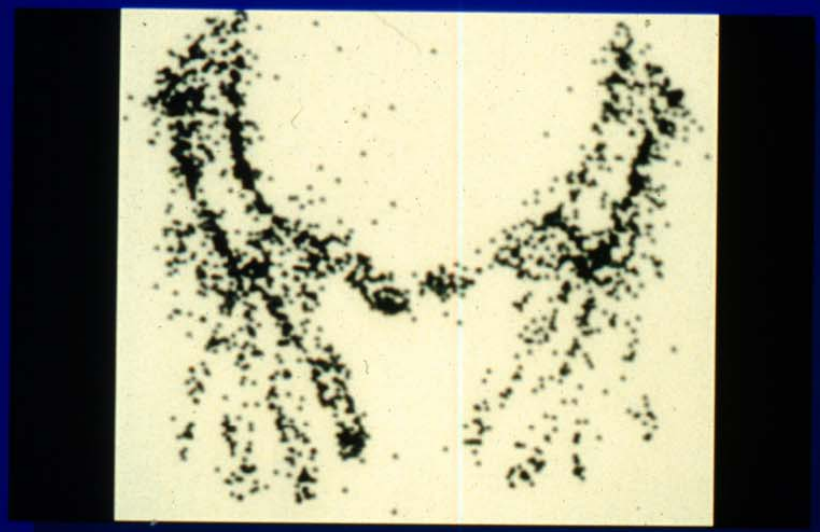
Analytical X-Ray Machine



Summary of Dose Rates at Critical Depths & Locations

Dose rate to fingers at a depth of 0.0025 mm	~9,000 rad/min
Dose rate at the soft tissue/bone interface	~5,600 rad/min
Dose rate to the lens of the eye at 20 cm directly into the beam port	100 rad/min

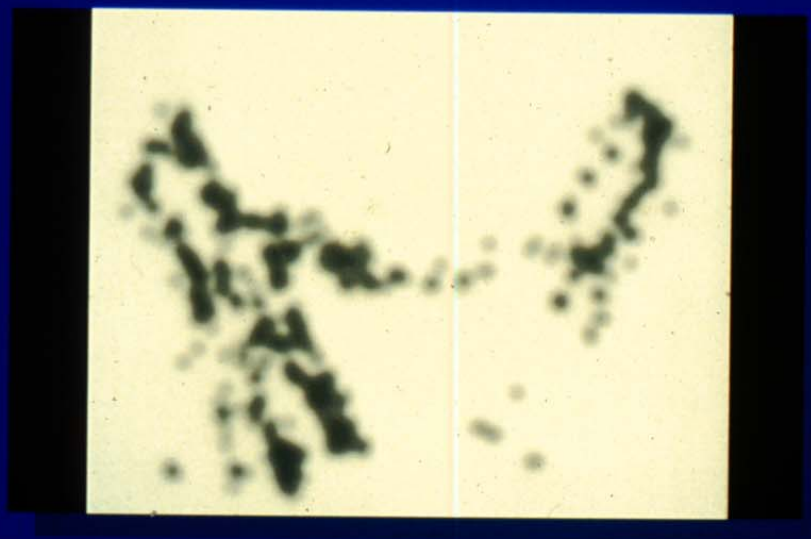
Day 4



Flow

Blood Pool

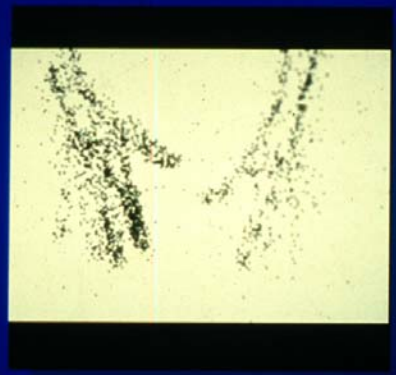
Day 39



Day 35

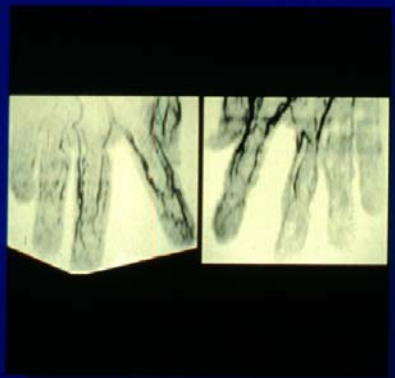
Day 16

Day 30

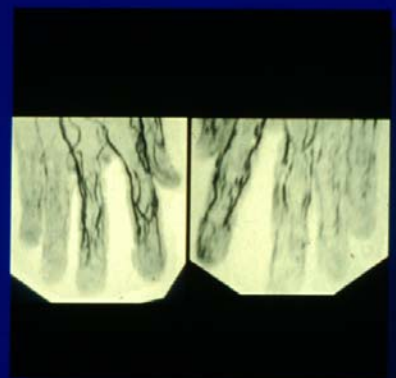


Day 14

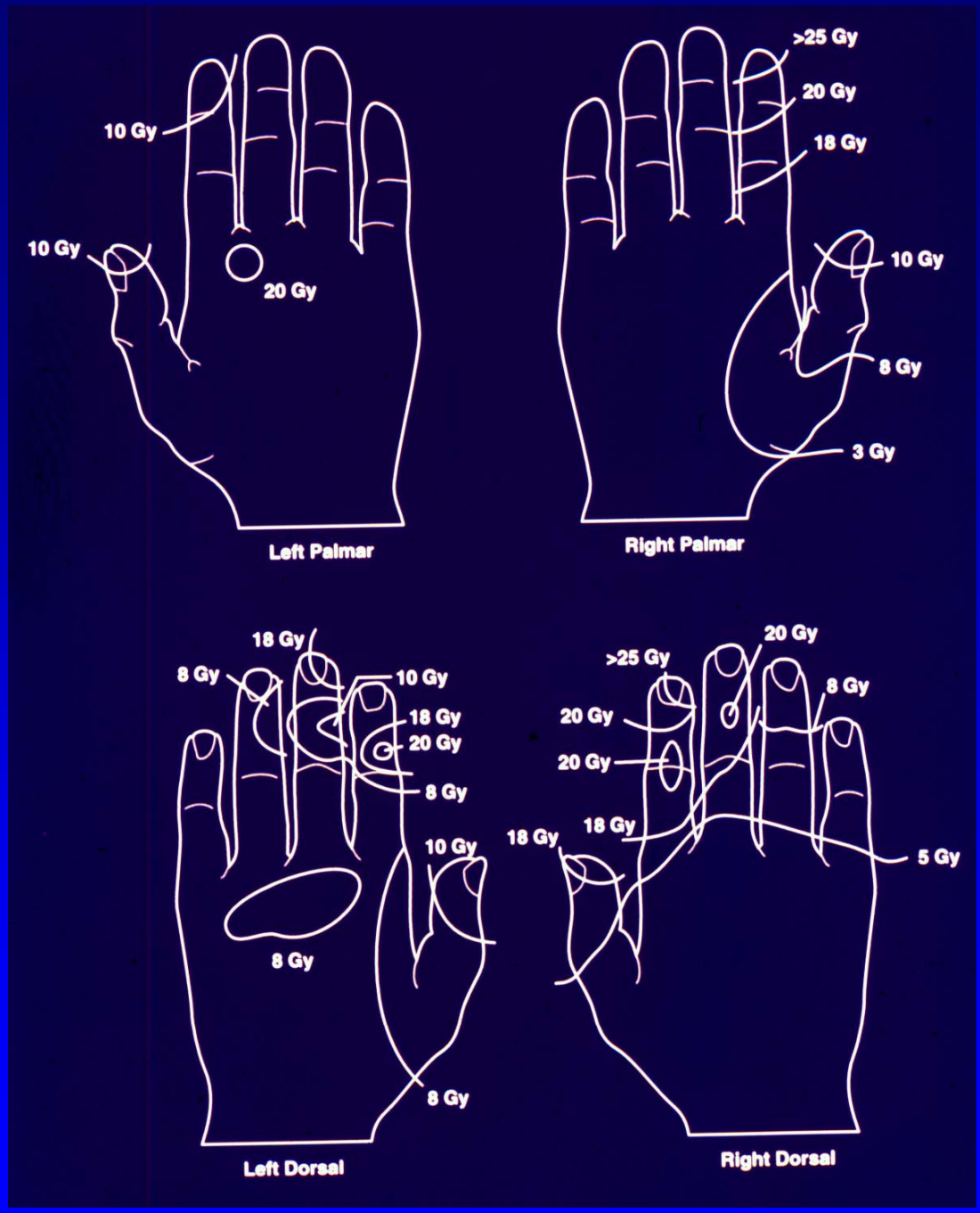
Day 35



Day 17



Day 34


10 Gy
10 Gy
20 Gy
Left Palmar
>25 Gy
20 Gy
18 Gy
10 Gy
8 Gy
3 Gy
Right Palmar
18 Gy
8 Gy
10 Gy
18 Gy
20 Gy
8 Gy
10 Gy
8 Gy
8 Gy
Left Dorsal
>25 Gy
20 Gy
8 Gy
20 Gy
20 Gy
18 Gy
18 Gy
5 Gy
Right Dorsal

THERAPY OF LOCAL RADIATION INJURIES

1 . **Prevent infection**
2 . **Drainage, debridement**
3 . **Grafting (split or full thickness)**
4 . **Possible microsurgery**
5 . **Amputation**

USEFUL STEPS IN EVALUATION OF LOCAL RADIATION INJURIES

- History and physical examination
- CBC with total lymphocyte count
- Serial color photographs
- Local hair loss
- Slit lamp of eyes
- Baseline x-ray
- Radionuclide blood flow study
- Possible sperm count
- Incident reconstruction